

# SELENON Gene

Subjects: Genetics & Heredity

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selenoprotein N

Keywords: genes

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## 1. Normal Function

The *SELENON* gene (also called *SEPN1*) provides instructions for making a protein called selenoprotein N. This protein is part of a family of selenoproteins, which have several critical functions within the body. Selenoproteins are primarily involved in chemical reactions called oxidation-reduction reactions, which are essential for protecting cells from damage caused by unstable oxygen-containing molecules. Although the exact function of selenoprotein N is unknown, it is likely involved in protecting cells against oxidative stress. Oxidative stress occurs when unstable molecules called free radicals accumulate to levels that damage or kill cells.

Selenoprotein N is highly active in many tissues before birth and may be involved in the formation of muscle tissue (myogenesis). The protein may also be important for normal muscle function after birth, although it is active at much lower levels in adult tissues. This protein is thought to play a role in maintaining an appropriate balance of calcium (calcium homeostasis) in cells. Calcium plays an important role in muscle movement.

## 2. Health Conditions Related to Genetic Changes

### 2.1. Multiminicore disease

At least 17 mutations in the *SELENON* gene have been identified in people with the classic form of multiminicore disease. This condition is named for a distinctive abnormality in the muscle fibers called minicores (which can only be seen with a microscope). In addition, affected individuals have muscle weakness, particularly in the muscles of the torso and neck (the axial muscles); abnormal curvature of the spine (scoliosis); and serious breathing problems. Many of the genetic changes that cause classic multiminicore disease lead to the production of an abnormally short version of selenoprotein N. Other mutations change single protein building blocks (amino acids) in critical regions of the protein. The effects of changes in the structure and function of selenoprotein N are unknown, and researchers are working to determine how these changes lead to muscle weakness and the other characteristic features of classic multiminicore disease.

### 2.2. Rigid spine muscular dystrophy

More than a dozen *SELENON* gene mutations have been found to cause rigid spine muscular dystrophy 1 (RSMD1). In people with this disorder, the muscles surrounding the spine weaken and waste away (atrophy), and the joints in the spine develop deformities called contractures that restrict movement. Affected children have limited ability to move their heads up and down or side to side. They also develop scoliosis and have serious breathing problems during sleep.

The *SELENON* gene mutations that cause RSMD1 are thought to reduce the amount of selenoprotein N or impair its activity in cells. It is unclear how a shortage of functional selenoprotein N affects the formation of muscle tissue or the function of muscles. Researchers are working to determine why axial muscles are particularly affected by *SELENON* gene mutations.

### 2.3. Other disorders

Mutations in the *SELENON* gene are involved in another rare muscle disorder called desmin-related myopathy with Mallory body-like inclusions. This disorder is characterized by the presence of small clusters of accumulated proteins in the muscle fibers. These abnormal regions can only be seen when muscle tissue is viewed under a microscope. The inclusions resemble an abnormality known as Mallory bodies. As in other *SELENON*-related muscle disorders (described

above), desmin-related myopathy with Mallory body-like inclusions is characterized by axial muscle weakness, spine stiffness, scoliosis, and serious breathing problems. Because they have a similar pattern of signs and symptoms and are caused by mutations in the same gene, many researchers believe that these conditions are all part of a single syndrome with variable signs and symptoms. Together, muscle diseases caused by *SELENON* gene mutations are known as *SELENON*-related (or *SEPN1*-related) myopathy. It is unclear why mutations in the *SELENON* gene cause the different muscle fiber abnormalities that distinguish these disorders.

### 3. Other Names for This Gene

- selenoprotein N, 1
- SELN
- SEPN1
- SEPN1\_HUMAN

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